

30. (New claim) The method of claim 29 wherein said antisense oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5.

31. (New claim) The method of claim 29 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>65</sub>.

32. (New claim) The method of claim 29 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>67</sub>.

33. (New claim) The method of claim 29 where in the isoform of said glutamic acid decarboxylase is a combination of GAD<sub>65</sub> and GAD<sub>67</sub>.

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REMARKS

Claims 1-22 are pending in the present application. Claims 5-8 and 13-22 have been cancelled without prejudice to their presentation in another application. Claims 1 and 9 have been amended, support for which can be found, for example, at page 8, lines 13-23 and page 11, lines 1-3 of the specification. New claims 23-33 have been added, support for which can be found at, throughout the specification and at page 8, line 30 to page 9, line 1 of the specification. No new matter has been added. Upon entry of the present amendment, claims 1-4, 9-12 and 23-33 will be pending. **Because the amendments to the claims and the new claims remove issues for appeal (i.e., enablement rejections), Applicant requests that they be entered into the record. See, M.P.E.P. § 714.12.**

As a preliminary matter, Applicants acknowledge receipt of the "Attachment for PTO-948" outlining changes for prosecution of applications containing drawings. To date, however, no Form PTO-948 has been received. Accordingly, the "Attachment for PTO-948" is not relevant in the present application.

**I. The Claimed Invention Is Enabled**

Claims 1-22 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to provide an enabling disclosure. The Office Action erroneously asserts that one skilled in the art would be required to perform undue experimentation to practice the entire scope of the claimed invention. Claims 5-8 and 13-22 have been cancelled without prejudice to their presentation in another application. Applicant traverses the rejection and requests reconsideration of remaining claims 1-4 and 9-12 and new claims 23-33 because one skilled in the art would be able to practice the claimed invention without being required to perform undue experimentation.

The enablement requirement of § 112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under § 112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971), is noteworthy:

The only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion. The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirements of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support. (emphasis added)

Any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974). The only reasoning provided in the Office Action is that 1) the claims are directed

to any antisense or triplex oligonucleotide; and 2) the claims are directed to any route of administration. Applicants has amended claims 1-4 and 9-12 and has presented new claims 23-33, which are amply enabled by the specification.

As a preliminary matter, the Office Action acknowledges that the specification is “enabling for administration of specific antisense oligonucleotides for therapeutic purposes claimed” (see paragraph 3 of the Office Action mailed in January, 2001). Thus, amended claims 1-4 and 9-12, which recite antisense oligonucleotides that have specific nucleotide sequences and which also recite administration via a cannula, are amply enabled.

New claims 23-27 are directed to methods of treating Parkinson’s disease in a mammal by administering a therapeutically effective amount of antisense oligonucleotide directed to glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase. Claims 23-27 are not directed to any route of administration but, instead, are directed to administration via a cannula to particular areas of the brain. The only remaining concern of the Office Action is, thus, the scope of the antisense oligonucleotides recited in claims 23-27 (*i.e.*, any antisense oligonucleotide that is directed to glutamic acid decarboxylase mRNA). Page 4 of the Office Action mailed in January, 2001, however, acknowledges that:

[The] Examiner does not disagree with the above statement stating that “the administration of any oligonucleotide to the target nucleic acid will inhibit, to varying efficiencies, the expression of the target...”

The only concern of the Office Action is in view of the functions claimed (*i.e.*, treatment of Parkinson’s disease). The Examiner is reminded that the claims are not directed to a method of “curing” Parkinson’s disease. Rather, administration of an antisense oligonucleotide that inhibits the expression of the target (*i.e.*, glutamic acid decarboxylase) to any extent can be used to “treat” Parkinson’s disease. Clearly, inhibition of glutamic acid decarboxylase to any extent in a mammal suffering from Parkinson’s disease would benefit such a mammal and would be better than not inhibiting glutamic acid decarboxylase at all. Inasmuch as the Office Action has already recognized that administration of any oligonucleotide to the target nucleic acid will inhibit, to varying

efficiencies, the expression of the target, new claims 23-27 are enabled. No amount of undue experimentation is required to practice the claimed invention.

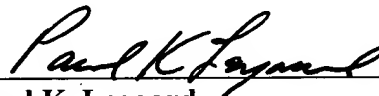
New claims 28-33 are directed to methods of downregulating glutamic acid decarboxylase in a mammal *in vivo* by administering an antisense oligonucleotide directed to glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula. Applicant's specification clearly demonstrates downregulation of glutamic acid decarboxylase in a mammal *in vivo* when an antisense oligonucleotide directed to glutamic acid decarboxylase mRNA is administered to the substantia nigra pars reticulata or internal globus pallidus via a cannula. Again, because administration of any oligonucleotide to the target nucleic acid will inhibit, to varying efficiencies, the expression of the target, new claims 28-33 are enabled. No amount of undue experimentation is required to practice the claimed invention.

In view of the foregoing, there is no reason to believe that one skilled in the art would be required to perform any amount of undue experimentation in order to make and use the claimed invention. Accordingly, Applicant requests that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

**II. Conclusion**

In view of the foregoing, Applicant respectfully submits that all pending claims are in condition for allowance. At a minimum, claims 1-4 and 9-12 are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 564-8906 if there are any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Respectfully submitted,



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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the Claims:**

Claims 1 and 9 have been amended as follows:

1. (Amended) A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of antisense oligonucleotide comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 to the substantia nigra pars reticulata via a cannula for the downregulation of glutamic acid decarboxylase.

9. (Amended) A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of antisense oligonucleotide comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5 to the internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase.

New claims 23-33 have been added as follows:

23. (New claim) A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of antisense oligonucleotide directed to glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase.

24. (New claim) The method of claim 23 wherein said antisense oligonucleotide is directed to the initiation codon of glutamic acid decarboxylase mRNA.

25. (New claim) The method of claim 23 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>65</sub>.

26. (New claim) The method of claim 23 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>67</sub>.

27. (New claim) The method of claim 23 where in the isoform of said glutamic acid decarboxylase is a combination of GAD<sub>65</sub> and GAD67.
28. (New claim) A method of downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide directed to glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula.
29. (New claim) The method of claim 28 wherein said antisense oligonucleotide is directed to the initiation codon of glutamic acid decarboxylase mRNA.
30. (New claim) The method of claim 29 wherein said antisense oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5.
31. (New claim) The method of claim 29 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>65</sub>.
32. (New claim) The method of claim 29 wherein the isoform of said glutamic acid decarboxylase is GAD<sub>67</sub>.
33. (New claim) The method of claim 29 where in the isoform of said glutamic acid decarboxylase is a combination of GAD<sub>65</sub> and GAD67.